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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,447	11/17/2003	Edward Roberts	A1479-3P US	9363

22466 7590 01/15/2010

ASTRA ZENECA PHARMACEUTICALS LP
GLOBAL INTELLECTUAL PROPERTY
1800 CONCORD PIKE
WILMINGTON, DE 19850-5437

EXAMINER	
BERNHARDT, EMILY B	
ART UNIT	**PAPER NUMBER**
1624	

MAIL DATE	DELIVERY MODE
01/15/2010	PAPER

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte EDWARD ROBERTS, NIKLAS PLOBECK, and
CLAES WAHLESTEDT

Appeal 2009-003460
Application 10/714,447
Technology Center 1600

Decided: January 15, 2010

Before TONI R. SCHEINER, DONALD E. ADAMS, and ERIC GRIMES, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

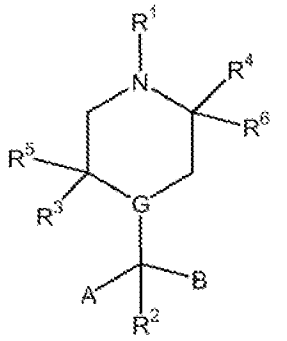
DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claim 19, the only claim pending in this application. We have jurisdiction under 35 U.S.C. § 6(b).

STATEMENT OF THE CASE

Claim 19 is directed to a compound of a particular formula and is reproduced below:

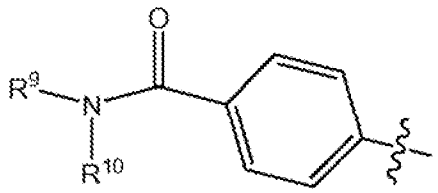
19. A compound of formula (I)



(I)

wherein G is a nitrogen atom;

A is:



wherein the phenyl ring of the A group is optionally substituted by one or two substituents independently selected from the group consisting of CH_3, CF_3 and halogen;

R^1 is selected from the group consisting of: H; a branched or straight C_1-C_6 alkyl; -CO(C_1-C_6 alkyl); and (C_1-C_6 alkyl)-B' wherein B' is a C_6, C_9 or C_{10} aryl or a 5 or 6 membered heteroaryl having a heteroatom selected from any of S, N and O and wherein the C_6, C_9 or C_{10} aryl and the 5 or 6 membered heteroaryl are optionally substituted with 1 or 2 substituents selected from CH_3 or halogen;

R^2 is selected from the group consisting of H and CH_3;

R^9, and R^{10}, are selected from the group consisting of H, a branched or straight C_1-C_6 alkyl and a C_2-C_6 alkenyl;

B is an C_6, C_9 or C_{10} aromatic; or a C_6, C_9 or C_{10} hydroaromatic; each being optionally substituted by 1 or 2 substituents independently selected from CH_3, CF_3, halogen, $(CH_2)_pCONR^7R^8$, $(CH_2)_pNR^7R^8$, $(CH_2,)_pCOR^7$, $(CH_2)_pCO_2R^7$, OR^7, $(CH_2)_pSOR^7$, $(CH_2)_pSO_2R^7$ and $(CH_2)_pSO_2NR^7R^8$;

wherein p is 0, 1, or 2, and wherein R^7 and R^8 are selected from: H; a branched or straight C_1-C_6 alkyl; or -CO(C_1-C_6 alkyl);

R^3, R^4, R^5, and R^6 are each H;

as well as pharmaceutically acceptable salts, hydrates, isoforms and isomers, other than positional isomers, thereof.

The Examiner relies on the following evidence:

Chang US 5,658,908 Aug. 19, 1997

Silvia N. Calderon, et al., *Probes for Narcotic Receptor Mediated Phenomena. 19.[1] Synthesis of (+)-4-[(αR)-α-((2S,5R)-4-Allyl-2,5-dimethyl-1-piperazinyl)-3-methoxybenzyl]-N,N-diethylbenzamide (SNC 80): A Highly Selective, Nonpeptide δ Opioid Receptor Agonist*, 37 J. Med. Chem. 2125-2128 (1994).

Edward J. Bilsky (Bilsky I), *Characterization of enantiomers of (±)BW373U86 and related compounds: highly selective non-peptidic delta opoid agonists*, 54 Reg. Peptides 25-26 (1994).

Edward J. Bilsky, et al. (Bilsky II), *SNC 80, A Selective, Nonpeptidic and Systemically Active Opioid Delta Agonist*, 273(1) J. Pharmacol. Exper. Ther. 359-366 (1995).

The rejection presented by the Examiner is as follows:

Claim 19 stands rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Calderon, Bilsky I, Bilsky II, and Chang.

We affirm.

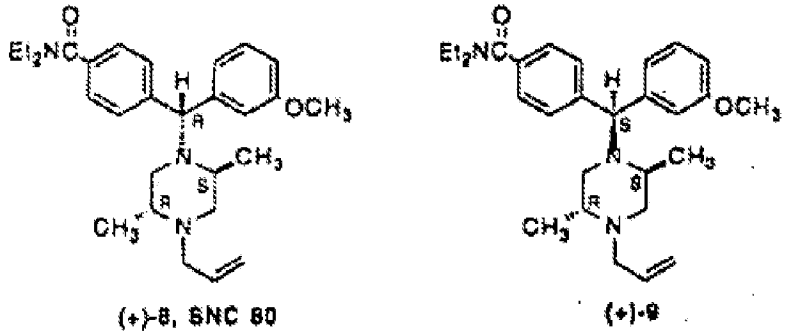
ISSUE

Have Appellants established error in the Examiner's prima facie case of obviousness?

FINDINGS OF FACT

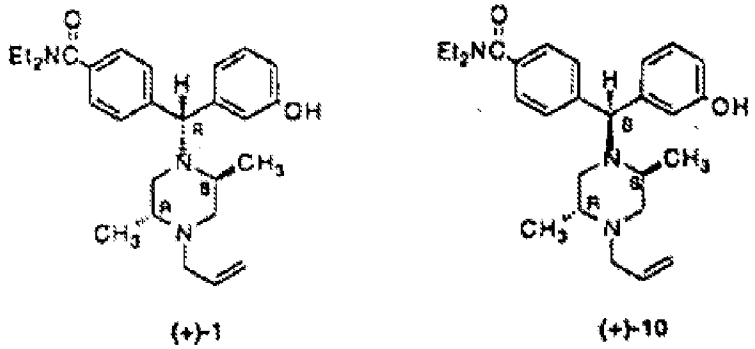
FF 1. Appellants do not dispute and therefore concede to the Examiner's finding that Calderon's "compounds 8 and 9 in reaction scheme 2" and "OH analogs 1 and 10" are similar to Appellants' claimed compound (Ans. 4-5).

FF 2. Calderon's Scheme 2, compounds 8 and 9 are reproduced below:



(Calderon 2126: col. 1, Scheme 2, compounds 8 and 9.)

FF 3. Calderon's Scheme 2, compounds 1 and 10 are reproduced below:



(Calderon 2126: col. 1, Scheme 2, compounds 1 and 10.)

FF 4. The Examiner finds that Bilsky I and Bilsky II teach "anisole derivatives, SNC80 and SNC 67[,] which are the same compounds (i.e. 8 and 9) discussed in Calderon" (Ans. 5).

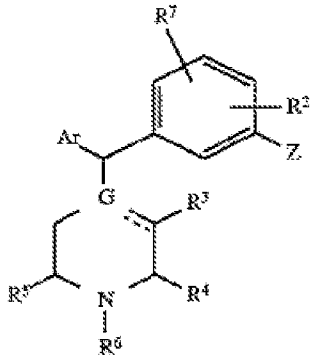
FF 5. Appellants do not dispute and therefore concede to the Examiner's finding that the compounds taught by Calderon, Bilsky I, and Bilsky II are useful in treating pain and have "activity at one or more opioid receptors" (*id.* at 4).

FF 6. The Examiner finds that the compounds taught by Calderon, Bilsky I, and Bilsky II do not anticipate Appellants' claimed compound due to the presence of an allyl at the R1 position of the prior art compounds rather than H, alkyl, aralkyl, etc., and "the presence of only hydrogen on piperazino carbons" of the claimed compounds (*id.* at 5).

FF 7. The Examiner finds that the compounds taught by Calderon, Bilsky I, and Bilsky II are "obvious variants" of Appellants' claimed compound "since the differences allyl vs[.] instant R1 as H, alkyl, aralkyl etc. are taught as interchangeable as well as methyl and hydrogen on piperazino carbons in similar compounds having the same use as described by the Chang patent" (*id.*).

FF 8. Chang teaches "compounds having utility as receptor-binding species, e.g., for mediating analgesia, and for combatting [sic] drug addiction, alcohol addiction, and drug overdose" (Chang, Abstract).

FF 9. Chang's compound is reproduced below:



(Chang, col. 3, ll. 20-30.)

FF 10. Chang defines "R3-R5" as "either H or Me and the choices for R6 . . . include hydrogen, alkyl, cycloalkyl, aralkyl" (Ans. 5).

FF 11. Chang teaches a number of illustrative compounds within the scope of Chang's invention (Chang, col. 7, l. 40 - col. 14, l. 29) and identifies these compounds as having "utility as exogenous receptor combinant compounds, i.e. compounds useful for binding with a receptor, such as delta receptor, mu receptor, sigma receptor, kappa receptor, or two or more of such receptors" (Chang, col. 14, ll. 30-35).

FF 12. The Examiner finds that Chang's compounds 3 {(-(α-(4-Allyl-1-piperazinyl)-4-propoxybenzyl)phenol)} and 4 {4'-(α-(4-Allyl-1-piperazinyl)-3-hydroxybenzyl)acetophenone} lack methyl groups on the piperazine carbons (Ans. 7; Chang, col. 7, ll. 44-46).

FF 13. The Examiner finds that Calderon's compounds 1, 8, 9, and 10 and the corresponding compounds taught by Bilsky I and Bilsky II are selective for the δ opioid receptor, "which is a desirable advantage as it minimizes physical dependence while promoting antinociceptive activity" (Ans. 5).

FF 14. The Examiner finds that Chang teaches selective opioid agonist compounds, including delta agonists when the "Y" position of Chang's compound "is para-substituted on the phenyl ring" (Ans. 5-6).

PRINCIPLES OF LAW

In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art. *In re Fritch*, 972 F.2d 1260, 1265 (Fed. Cir. 1992). On appeal to this Board, Appellants must show that the Examiner has not sustained the required burden. *See Ex parte Yamaguchi*, 88 USPQ2d 1606, 1608 and 1614 (BPAI 2008) (precedential); *Ex parte Fu*, 89 USPQ2d 1115, 1118 and 1123 (BPAI 2008) (precedential).

"The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). It is proper to "take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* at 418. *See also id.* at 421 ("A person of ordinary skill is also a person of ordinary creativity, not an automaton.").

"[I]n a section 103 inquiry, 'the fact that a specific [embodiment] is taught to be preferred is not controlling, since all disclosures of the prior art, including unpreferred embodiments, must be considered.'" *Merck & Co. Inc. v. Biocraft Laboratories, Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989) (quoting *In re Lamberti*, 545 F.2d 747, 750 (CCPA 1976)); *see also In re Mills*, 470 F.2d 649, 651 (CCPA 1972) ("All the disclosures in a reference must be evaluated, including nonpreferred embodiments, and a reference is not limited to the disclosure of specific working examples." (citations omitted)).

ANALYSIS

Based on the foregoing findings of fact (FF) the Examiner concludes that:

> [I]t would have been obvious to one skilled in the art at the time the instant invention was made to replace the aforementioned groups in . . . [Calderon, Bilsky I, and Bilsky II] with those present herein at instant R1 and R3-R6 and in so doing obtain additional compounds for treating pain in view of the equivalency teachings outlined above in . . . [Chang].

(Ans. 6.)

Appellants contend that the compounds taught by Calderon, Bilsky I, and Bilsky II have "dimethyl groups substituted on the carbons of the central piperazine ring" (App. Br. 5; Reply Br. 2). Appellants contend that "at the time the present application was filed, a person of ordinary skill in the art upon viewing Chang . . . as a whole would not have been motivated to modify the compounds disclosed in Calderon . . . and/or Bilsky . . . so as to arrive at the presently claimed compounds" (App. Br. 6). We are not persuaded.

The Examiner found and Appellants do not dispute that the compounds taught by Chang are structurally similar to those taught by Calderon, Bilsky I, and Bilsky II (FF 7). The Examiner finds that Chang teaches two compounds that lack methyl groups on the piperazine carbons (FF 12). Chang teaches that these compounds are useful "as exogenous receptor combinant compounds" (FF 11). Accordingly, we find no error in the Examiner's conclusion that it would have been obvious to substitute hydrogen for the methyl groups on the piperazine ring of the compounds taught by Calderon, Bilsky I, and Bilsky II. Accordingly, we are not

persuaded by Appellants' contentions regarding *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007). On this record, Chang provided the suggestion to make the modification proposed by the Examiner.

Appellants contend that contrary to the Examiner's assertion, Chang teaches that methyl and hydrogen did not behave equivalently and were not interchangeable (App. Br. 6; *see also* Reply Br. 1). In support of this contention Appellants direct attention to the prosecution record of Chang, wherein Chang "stated in relevant part in reliance on a 132 declaration . . . [that] comparing compounds in which the piperazine ring is substituted with two methyl groups, with those that do not have a substituent on any of the carbon atoms of the piperazine ring, show[s] a general trend in which the substituted compounds have significantly greater opioid activity" (App. Br. 7 (emphasis removed); *see also* Reply Br. 2). From this Appellants contend that "it is difficult to predict what impact a hydrogen-methyl exchange will have on the delta activity of the resulting piperazine derivative" (Reply Br. 3). We are not persuaded.

There is no requirement in Appellants' claim 19 that the compound has opioid activity, much less δ opioid activity or opioid activity that is greater or less than another compound. In addition, the data in Chang's declaration show that compounds with an unsubstituted piperazine ring have opioid activity. Chang's assertion that compounds with methyl groups on the piperazine ring have greater activity than those that do not does not support a conclusion that compounds lacking methyl groups on the piperazine ring do not have activity or would not have been suggested from the combination of Calderon, Bilsky I, Bilsky II, and Chang.

We are also not persuaded by Appellants' contention that Chang disclosed a preference for compounds that "have methyl substituted on the piperazinyl ring at at least one of the R^3, R^4 and R^5 positions" (App. Br. 7; see also Reply Br. 3 ("Appellants assert Chang et al.'s failure to include such compounds in the Example section or within the scope of the broadest claim further supports Chang et al.'s own statements that hydrogen and methyl are not equivalent")). A reference is not limited to its preferred embodiments (*see* Ans. 7-8). *Mills*, 470 F.2d at 651.

CONCLUSION OF LAW

Appellants failed to establish error in the Examiner's prima facie case of obviousness. The rejection of claim 19 under 35 U.S.C. § 103(a) as unpatentable over the combination of Calderon, Bilsky I, Bilsky II, and Chang is affirmed.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

alw

ASTRA ZENECA PHARMACEUTICALS LP
GLOBAL INTELLECTUAL PROPERTY
1800 CONCORD PIKE
WILMINGTON, DE 19850-5437